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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
SPECTOR, LORRAINE	

ART UNIT	PAPER NUMBER
1647	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/517,028	BUNSCHOTEN ET AL.	
	Examiner	Art Unit	
	Lorraine Spector	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 February 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,5-8 and 12-20* is/are pending in the application.

4a) Of the above claim(s) *14 and 15* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,5-8,12,13 and 16-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-3,5-8 and 12-20* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 2/17/2009 has been entered.

Your application has been re-docketed. Please direct all further correspondence to Examiner Lorraine Spector, in Art Unit 1647.

Claim Objections

Claim 2 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. The independent claim, claim 1, is drawn to a method of "controlled ovarian hyperstimulation". The method steps of claim 2 do not relate to ovarian hyperstimulation, but rather are subsequent steps in a method of *in vitro* fertilization.

Claim Interpretation

While claim 1 does not state when the first three hormones are to be administered, claims, for example claim 5, make clear that they do not need to be administered simultaneously, or even on the same days.

Due to the inclusion of the term “at least” in claim 5, the administration of the GnRH antagonist may begin at any step in the process prior to the largest developing ovarian follicle reaching 14 mm diameter.

Many of the claims specify that the LH is "recombinant", "obtained from a recombinant cell line", or the CG is of urinary or recombinant origin. Such product by process recitations are given weight only to the extent that they materially affect the product in question.

Many claims, for example claims 6-8 and 20, recite that something is administered "at least during the period starting X days after" an event. It is noted that this language does not require treatment to being on day X, but merely on or after day X.

Claims such as claims 5-8, which specify that an agent is administered "at least" during a certain period do not require that the agent be administered for the entire period, but merely some portion thereof.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-3, 5-8, 12, 13 ad 16-20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is indefinite because it apparently comprises two steps, the first in which an FSH substance a GnRH antagonist and LH are administered, "followed by" a step in which an ML substance is administered, which can be recLH, urinary CG, recombinant CG, GnRH, or mixtures thereof. However, there is no relationship between the two steps other than the broad and indefinite "followed by". It is not clear *when* the second step should follow the first, either in terms of timing or a biological endpoint.

Claim 2 fails to state when in the method of claim 1 the additional steps are to be performed.

Claim 3 is indefinite because (a) claim 1, from which it depends, has two possible steps of administering LH, and it is not clear to which claim 3 refers, (b) it is not clear as to a litre of *what* the LH level is measured, and (c) claim 1 recites a daily sub-q dose of LH between 1 and 40 IU per Kg bodyweight, whereas claim 3 represents dosage as "more than 1 IU LH/litre" of

blood serum, and it is not clear how to reconcile these two limitations. Claim 16 is similarly indefinite.

Claim 5 is indefinite because there is no antecedent basis in claim 1 for measurement of ovarian follicles. Claims 18 and19 are similarly indefinite.

Claim 13 is indefinite because it recites administration of all three active agents of the first part of the claim daily. It is not clear whether they are all administered on the *same* days, or on different days/regimes, as in some of the other claims that depend from claim 1.

The remaining claims are rejected for depending on an indefinite claim.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-3, 5-8, 12, 13 and 16-20 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The claims recite precursors of ganirelix or cetrorelix. No such precursors are described in the specification as originally filed, nor could the examiner find examples of such in the patent literature, such that they are not considered to be well known in the art such that the person of ordinary skill in the art would immediately recognize what structures are implied.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an

> international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1, 2, 6-8, 12-13, and 18-20 are rejected under 35 U.S.C. 102(e) as being anticipated by Hillier et al., U.S. Patent No. 7,341,989.

Hillier et al., which merits a foreign priority date of 12/12/2001 teaches the use of LH in COH (title).

At column 5, Hillier discloses the administration of a short regimen of LH at the beginning of the stimulatory phase, followed by FSH administration; see lines 29-44. The LH dosage is given as 5-300 (lines 56-67), which overlaps the claimed range of 1-40 IU (claim 1). At column 6 beginning at line 64, Hillier et al. state that the LH priming regimen may be used in conjunction with treatment with a GnRH antagonist. Also mentioned is that the LH and FSH may overlap by one day. In the following paragraph, it is disclosed that a single administration of LH may suffice, and that FSH may be commenced simultaneously or on the following day. LH may also be administered up to four days. Also taught therein is that LH may be administered on a daily or semi-daily basis for up to four days, with as little as one day overlap with FSH administration; as FSH administration is disclosed as being up to six days, this meets the limitations of claim 8 and 20. Cetrorelix and Ganirelix are specifically mentioned as GnRH antagonists at the top of column 7. Also disclosed therein is that FSH is given starting on day 1-3 of menstruation, and a GnRH antagonist at FSH stimulation day 6, meeting the limitations of claims 6 and 18-19. The advantages of the regime are disclosed at column 7 beginning at line 24 as allowing reduction in FSH dosage, or earlier triggering of ovulation. Paragraph 2 of column 6 describes a dosage regime consistent with claim 7. Recombinant LH, which would necessarily be produced by a recombinant cell line, is disclosed at the top of column 9, meeting the limitations of claim 12. With respect to claim 13, as the claim cannot be fully interpreted, the broadest reasonable interpretation is that the three hormones are administered at least once a day, which is met by Hillier, but not necessarily on the same days.

Claim Rejections, 35 U.S.C. §102 and/or 103(a)

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 3, 5, 16 and 17 are rejected under 35 U.S.C. 102(e) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Hillier et al., U.S. Patent No. 7,341,989.

The examiner is unable to determine what the serum concentrations of LH would be following Hillier's guidance (claims 3 and 16) . As column 6 discloses starting at line 25 the FSH administration is generally continued until there are at least 3 follicles >16 mm, the GnRH antagonist administration appears to be within the period stated in claim 5, although the Examiner is not able to unequivocally determine such.. Similarly, the Examiner cannot determine whether Hillier's doses could achiever the equivalency to the amounts recited in claim 17. Claim 5 contains specific limitations as to when the GnRH is administered, that also cannot be unequivocally determined from the Hillier disclosure.

Under such circumstances, where the method seems to be identical, then the burden shifts to applicant to provide evidence that the prior art would neither anticipate nor render obvious the claimed invention. Note the case law of In re Best 195 USPQ 430, 433 (CCPA 1977).

In the event that there is a difference between the instant claims and Hillier, the Examiner maintains that any such difference represents merely routine optimization of the method; both

the Hillier patent and the instant specification demonstrate that dosage amounts and regimes vary with patients, no two patients being the same.

It is noted that the instant specification contains only two working examples; Example 1 used daily sub-q administration from day 6 of recombinant FSH treatment up to and including the day of urinary hCG treatment, using .25 or 2 mg of cetrorelix, or 2 mg cetrorelix with 400 IU recLH. Recombinant FSH treatment was started at day 2 or 3 of menses. "Starting at day 6, blood samples for hormone analysis are taken once every two days prior to drug administration." This is evidence that the regime must be tailored to each patient. Further, the Examples are not commensurate in scope with the claims, further indicating that dosage amount and regime is considered to be within the purview of the skilled artisan. Accordingly, Hillier et al. teach at least as much as the instant specification.

Conclusion

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Lorraine M. Spector. Dr. Spector can normally be reached Monday from 9-5, and Tuesday, Thursday and Friday, 9:00 A.M. to 3:00 P.M. at telephone number 571-272-0893.

If attempts to reach the Examiner by telephone are unsuccessful, please contact the Examiner's supervisor, Dr. Manjunath Rao, at telephone number 571-272-0939.

Certain papers related to this application may be submitted to Technology Center 1600 by facsimile transmission The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). NOTE: If Applicant does submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Official papers filed by fax should be directed to **571-273-8300**. Faxed draft or informal communications with the examiner should be directed to ***571-273-0893.***

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Lorraine Spector, Ph.D.
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Art Unit 1647